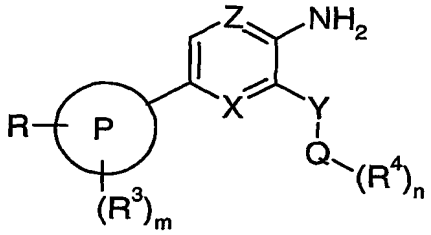
CLAIMS

1. A compound having the formula I



(I)

wherein:

Z is N;

Y is $CONR^5$, NR^5CO, SO_2NR^5, NR^5SO_2, CH_2NR^5, NR^5CONR^5, CH_2CO, CO or CH_2O;

X is CH or N;

P is phenyl or a 5 or 6 membered heteroaromatic ring containing one or more heteroatoms selected from N, O or S and said phenyl ring or 5 or 6 membered heteroaromatic ring may optionally be fused with a 5 or 6 membered saturated, partially saturated or unsaturated ring containing atoms independently selected from C, N, O or S;

Q is C_{1-6}alkyl, C_{2-6}alkenyl or C_{2-6}alkynyl;

R is CHO, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6}alkyl$(SO_2)NR^1R^2$, OC_{0-6}alkyl$(SO_2)NR^1R^2$, OC_{1-6}alkyl$(SO)NR^1R^2$, C_{1-6}alkyl$(SO)NR^1R^2$, C_{0-6}alkyl$NR^1(SO)R^2$, OC_{1-6}alkyl$NR^1(SO)R^2$, C_{0-6}alkyl$NR^1(SO_2)NR^1R^2$, OC_{1-6}alkyl$NR^1(SO_2)R^2$, C_{0-6}alkyl$(SO_2)C_{1-6}$alkylNR^1R^2, OC_{0-6}alkyl$(SO_2)C_{1-6}$alkylNR^1R^2, C_{0-6}alkyl$(SO)C_{1-6}$alkylNR^1R^2, OC_{1-6}alkyl$(SO)C_{1-6}$alkylNR^1R^2, C_{0-6}alkylSC_{1-6}alkylNR^1R^2, OC_{1-6}alkylSC_{1-6}alkylNR^1R^2, OC_{1-6}alkylOC_{1-6}alkyl, C_{1-6}alkylOC_{1-6}alkylNR^1R^2, OC_{1-6}alkylOC_{1-6}alkylNR^1R^2, C_{0-6}alkyl$CONR^{10}R^{11}$, OC_{0-6}alkyl$CONR^1R^2$, OC_{1-6}alkylNR^1R^2, C_{0-6}alkyl$NR^{10}(CO)R^{11}$, OC_{1-6}alkyl$NR^1(CO)R^2$, C_{0-6}alkyl$NR^{11}(CO)R^{10}$, C_{0-6}alkylCOR^{11}, OC_{1-6}alkylCOR^1, C_{0-6}alkyl$NR^{10}R^{11}$, C_{0-6}alkyl$O(CO)R^{11}$, OC_{1-6}alkyl$O(CO)R^1$, C_{0-6}alkyl$C(NR^{10})NR^{10}R^{11}$, C_{0-6}alkyl$C(NR^{11})N(R^{10})_2$, OC_{0-6}alkyl$C(NR^1)NR^1R^2$, C_{0-6}alkyl$NR^{10}(CO)OR^{11}$, OC_{1-6}alkyl$NR^1(CO)OR^2$,

C_{0-6}alkylNR^{11}(CO)OR^{10}, OC_{1-6}alkylCN, NR^{1}OR^2, C_{0-6}alkyl(CO)OR^8, OC_{1-6}alkyl(CO)OR^1, NR^1(CO)NR^{1}R^2, NR^1(CO)(CO)R^2, NR^1(CO)(CO)NR^{1}R^2, OR^{12} or SO_3R^1;

R^1 and R^2 are independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylheterocycloalkyl , C_{1-6}alkylNR^{6}R^7, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylheterocycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl may be substituted by one or more A;

R^1 and R^2 may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

R^3 is independently selected from halogen, nitro, CHO, C_{0-6}alkylCN, OC_{1-6}alkylCN, C_{0-6}alkylOR^6, OC_{1-6}alkylOR^6, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6}alkylNR^{6}R^7, OC_{1-6}alkylNR^{6}R^7, OC_{1-6}alkylOC_{1-6}alkylNR^{6}R^7, NR^{6}OR^7, C_{0-6}alkylCO_2R^6, OC_{1-6}alkylCO_2R^6, C_{0-6}alkylCONR^{6}R^7, OC_{1-6}alkylCONR^{6}R^7, OC_{1-6}alkylNR^6(CO)R^7, C_{0-6}alkylNR^6(CO)R^7, O(CO)NR^{6}R^7, NR^6(CO)OR^7, NR^6(CO)NR^{6}R^7, O(CO)OR^6, O(CO)R^6, C_{0-6}alkylCOR^6, OC_{1-6}alkylCOR^6, NR^6(CO)(CO)R^6, NR^6(CO)(CO)NR^{6}R^7, SR^6, C_{0-6}alkyl(SO_2)NR^{6}R^7, OC_{1-6}alkylNR^6(SO_2)R^7, OC_{0-6}alkyl(SO_2)NR^{6}R^7, C_{0-6}alkyl(SO)NR^{6}R^7, OC_{1-6}alkyl(SO)NR^{6}R^7, SO_3R^6, C_{0-6}alkylNR^6(SO_2)NR^{6}R^7, C_{0-6}alkylNR^6(SO)R^7, OC_{1-6}alkylNR^6(SO)R^7, OC_{0-6}alkylSO_2R^6, C_{0-6}alkylSO_2R^6, C_{0-6}alkylSOR^6, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl may be optionally substituted by one or more A;

R^4 is independently selected from halogen, nitro, CHO, CN, OC_{1-6}alkylCN, OR^6, OC_{1-6}alkylOR^6, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, NR^{6}R^7, OC_{1-6}alkylNR^{6}R^7, NR^{6}OR^7, CO_2R^6, OC_{1-6}alkylCO_2R^6, CONR^{6}R^7, OC_{1-6}alkylCONR^{6}R^7, OC_{1-6}alkylNR^6(CO)R^7, NR^6(CO)R^7, O(CO)NR^{6}R^7, NR^6(CO)OR^7, NR^6(CO)NR^{6}R^7, O(CO)OR^6, O(CO)R^6, COR^6, OC_{1-6}alkylCOR^6, NR^6(CO)(CO)R^6, NR^6(CO)(CO)NR^{6}R^7, SR^6, (SO_2)NR^{6}R^7, OC_{1-6}alkylNR^6(SO_2)R^7, OC_{0-6}alkyl(SO_2)NR^{6}R^7, (SO)NR^{6}R^7, OC_{1-6}alkyl(SO)NR^{6}R^7, SO_3R^6, NR^6(SO_2)NR^{6}R^7, NR^6(SO)R^7, OC_{1-6}alkylNR^6(SO)R^7, OC_{0-6}alkylSO_2R^6, SO_2R^6, SOR^6, C_{3-6}cycloalkyl, phenyl, a 5 or 6 membered heteroaromatic ring containing one or

more heteroatoms independently selected from N, O, or S, or a 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O, or S which heterocyclic group may be saturated or unsaturated, and said phenyl ring or 5 or 6 membered heteroaromatic ring or 5 or 6 membered heterocyclic ring may optionally be fused with a 5 or 6 membered saturated, partially saturated or unsaturated ring containing atoms independently selected from C, N, O or S wherein any C_{3-6}cycloalkyl, phenyl, 5 or 6 membered heteroaromatic ring with one or two heteroatoms selected independently from N, O, or S or a 5 or 6 membered heterocyclic containing one or two heteroatoms selected independently from N, O, or S; may be optionally be substituted by one or more A;

m is 0, 1, 2, 3 or 4;

n is 0, 1, 2, 3 or 4;

R^5 is hydrogen or C_{1-6}alkyl

R^6 and R^7 are independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl and C_{1-6}alkylNR^8R^9;

R^6 and R^7 may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A and wherein a CH_2 group may optionally be replaced by a CO group;

R^8 and R^9 are independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl;

R^8 and R^9 may together form a 5 or 6 membered heterocyclic ring containing one or more heteroatoms selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

R^{10} is hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl or C_{1-6}alkylNR^8R^9;

R^{11} is C_{1-6}alkylNR^8R^9;

R^{10} and R^{11} may together form a 5 or 6 membered heterocyclic ring containing one or more heteroatoms selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

R^{12} is a 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A; wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl,

C_{0-6}alkylheterocycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl defined under R^5 to R^{12} may be substituted by one or more A;

A is halo, oxo (=O), nitro, CHO, CN, OR^6, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6}alkylNR^6R^7, OC_{1-6}alkylNR^6R^7, CO_2R^8, $CONR^6R^7$, $NR^6(CO)R^6$, $O(CO)R^6$, COR^6, SR^6, $(SO_2)NR^6R^7$, $(SO)NR^6R^7$, SO_3R^6, SO_2R^6 or SOR^6;

as a free base or a pharmaceutically acceptable salt, solvate or solvate of a salt thereof.

2. A compound according to claim 1, wherein Z and X is N; P is phenyl; R is C_{0-6}alkyl$(SO_2)NR^1R^2$; and m is 0.

3. A compound according to claim 2, wherein R^1 and R^2 in C_{0-6}alkyl$(SO_2)NR^1R^2$ together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms selected from N, O or S.

4. A compound according to claim 3, wherein said heterocyclic ring comprises one or more N heteroatoms and said heterocyclic ring is optionally substituted by A, preferably a C_{1-6}alkyl.

5. A compound according to any one of claims 1 to 4, wherein Y is $CONR^5$; R^5 is hydrogen; Q is C_{1-6}alkyl; R^4 is selected from: phenyl, 5 or 6 membered heteroaromatic ring containing one or more heteroatoms independently selected from N, O, or S or a 5 or 6 membered heterocyclic ring containing one or two heteroatoms selected independently from N, O, or S which heterocyclic group may be saturated or unsaturated, CN, OR^6, SO_2R^6, $NR^6(CO)R^7$, $(SO_2)NR^6R^7$, and $CONR^6R^7$; and n is 1; said phenyl or 5 or 6 membered heterocyclic ring optionally substituted by A.

6. A compound according to claim 5, wherein A is selected from OR^6, C_{1-6}alkyl, oxo (=O) and nitro; and R^6 and/or R^7 is selected from C_{1-6}alkyl and hydrogen.

7. A compound which is

3-Amino-*N*-(2-cyanoethyl)-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide;
3-Amino-*N*-(3-amino-3-oxopropyl)-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide;
3-Amino-*N*-(2-nitrobenzyl)-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide
3-Amino-*N*-(2-methoxybenzyl)-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide;
3-Amino-*N*-(3-morpholin-4-ylpropyl)-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide;
3-Amino-*N*-[3-(4-methylpiperazin-1-yl)propyl]-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide;

as a free base or a pharmaceutically acceptable salt, solvate or solvate of a salt thereof;

3-Amino-*N*-(2-morpholin-4-ylethyl)-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide hydrochloride;
3-Amino-*N*-[2-(1*H*-imidazol-4-yl)ethyl]-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide hydrochloride;
3-Amino-*N*-[3-(1*H*-imidazol-1-yl)propyl]-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxamide hydrochloride;
3-Amino-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}-*N*-(2-thien-2-ylethyl)pyrazine-2-carboxamide hydrochloride;
3-Amino-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}-*N*-(thien-2-ylmethyl)pyrazine-2-carboxamide hydrochloride;
3-Amino-*N*-(2-methoxyethyl)-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide hydrochloride;
3-Amino-*N*-(3-methoxypropyl)-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide hydrochloride;
3-Amino-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}-*N*-[3-(2-oxopyrrolidin-1-yl)propyl]pyrazine-2-carboxamide hydrochloride;
3-Amino-*N*-(cyanomethyl)-6-{4-[(4-methylpiperazin-1-yl)sulfonyl]phenyl}pyrazine-2-carboxamide dihydrochloride;

3-Amino-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-*N*-[2-(1*H*-pyrrol-1-yl)ethyl]-2-pyrazinecarboxamide hydrochloride;
3-Amino-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-*N*-[2-(methylsulfonyl)ethyl]-2-pyrazinecarboxamide hydrochloride;
N-[2-(Acetylamino)ethyl]-3-amino-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-2-pyrazinecarboxamide hydrochloride;
3-Amino-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-*N*-[2-(2-oxo-1-imidazolidinyl)ethyl]-2-pyrazinecarboxamide hydrochloride;
3-Amino-*N*-[2-(aminosulfonyl)ethyl]-6-[4-[(4-methyl-1-piperazinyl)sulfonyl]phenyl]-2-pyrazinecarboxamide hydrochloride;
or as a free base or an alternative pharmaceutically acceptable salt, solvate or solvate of a salt thereof;

8. A pharmaceutical formulation comprising as active ingredient a therapeutically effective amount of the compound according to any one of claims 1 to 7 in association with pharmaceutically acceptable carriers or diluents.

9. The pharmaceutical formulation according to claim8 for use in the prevention and/or treatment of conditions associated with glycogen synthase kinase-3.

10. A compound as defined in any one of claims 1 to 7 for use in therapy.

11. Use of a compound according to any one of claims 1 to 7 in the manufacture of a medicament for prevention and/or treatment of conditions associated with glycogen synthase kinase-3.

12. Use of a compound according to any one of claims 1 to 7 in the manufacture of a medicament for prevention and/or treatment of dementia, Alzheimer's Disease, Parkinson's Disease, Frontotemporal dementia Parkinson's Type, Parkinson dementia complex of Guam, HIV dementia, diseases with associated neurofibrillar tangle pathologies and dementia pugilistica.

13. The use according to claim 12 wherein the prevention and/or treatment is for Alzheimer's Disease.

14. Use of a compound according to any one of claims 1 to 7 in the manufacture of a medicament for prevention and/or treatment of amyotrophic lateral sclerosis, corticobasal degeneration, Down syndrome, Huntington's Disease, postencephelatic parkinsonism, progressive supranuclear palsy, Pick's Disease, Niemann-Pick's Disease, stroke, head trauma and other chronic neurodegenerative diseases, Bipolar Disease, affective disorders, depression, schizophrenia, cognitive disorders, hair loss and contraceptive medication, Type I and Type II diabetes, diabetic neuropathy and diabetes related disorders.

15. Use of a compound according to claim 14, wherein the prevention and/or treatment is Type I and Type II diabetes, diabetic neuropathy and diabetes related disorders.

16. Use of a compound according to any one of claims 1 to 7 in the manufacture of a medicament for prevention and/or treatment of predemented states, Mild Cognitive Impairment, Age-Associated Memory Impairment, Age-Related Cognitive Decline, Cognitive Impairement No Dementia, mild cognitive decline, mild neurocognitive decline, Late-Life Forgetfulness, memory impairment and cognitive impairment, vascular dementia, dementia with Lewy bodies, Frontotemporal dementia and androgenetic alopecia.

17. A method of prevention and/or treatment of conditions associated with glycogen synthase kinase-3, comprising administrering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound of formula I as defined in any one of claims 1 to 7.

18. A method of prevention and/or treatment of dementia, Alzheimer's Disease, Parkinson's Disease, Frontotemporal dementia Parkinson's Type, Parkinson dementia complex of Guam, HIV dementia, diseases with associated neurofibrillar tangle pathologies and dementia pugilistica, comprising administrering to a mammal, including

man in need of such prevention and/or treatment, a therapeutically effective amount of a compound of formula **I** as defined in any one of claims 1 to 7.

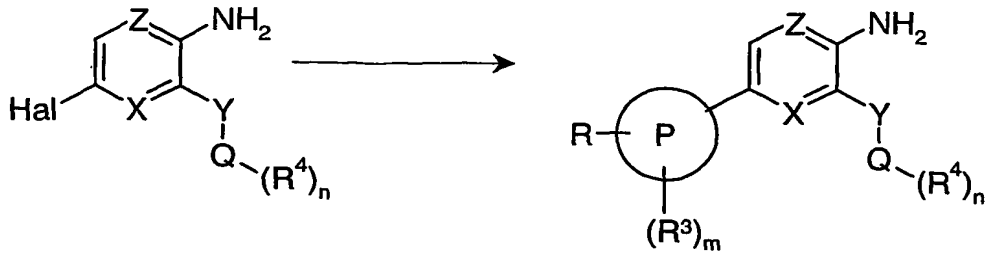
19. The method according to claim 18, wherein the prevention and/or treatment is for Alzheimer's Disease.

20. A method of prevention and/or treatment of amyotrophic lateral sclerosis, corticobasal degeneration, Down syndrome, Huntington's Disease, postencephelatic parkinsonism, progressive supranuclear palsy, Pick's Disease, Niemann-Pick's Disease, stroke, head trauma and other chronic neurodegenerative diseases, Bipolar Disease, affective disorders, depression, schizophrenia, cognitive disorders, hair loss and contraceptive medication, Type I and Type II diabetes, diabetic neuropathy and diabetes related disorders, comprising administrering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound of formula **I** as defined in any one of claims 1 to 7.

21. The method according to claim 18, wherein the prevention and/or treatment is Type I and Type II diabetes, diabetic neuropathy and diabetes related disorders.

22. A method of prevention and/or treatment of predemented states, Mild Cognitive Impairment, Age-Associated Memory Impairment, Age-Related Cognitive Decline, Cognitive Impairement No Dementia, mild cognitive decline, mild neurocognitive decline, Late-Life Forgetfulness, memory impairment and cognitive impairment, vascular dementia, dementia with Lewy bodies, Frontotemporal dementia and androgenetic alopecia, comprising administrering to a mammal, including man in need of such prevention and/or treatment, a therapeutically effective amount of a compound of formula **I** as defined in any one of claims 1 to 7.

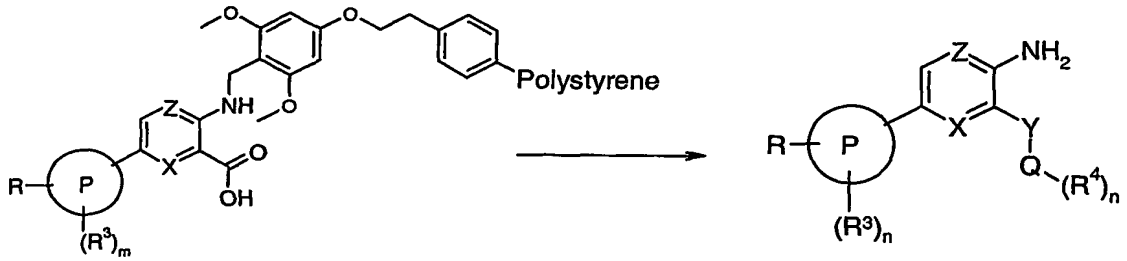
23. A process for the preparation of a compound of formula **I** according to claim 1, wherein Y, X, Z, P, Q, R, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, A, m and n are defined as in formula **I**, comprising of de-halogen coupling of a compound of formula **IV** with an appropriate aryl species;



(IV) (I)

to give a compound of formula I.

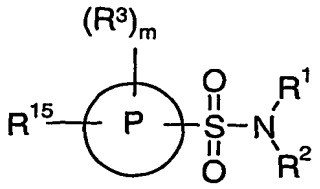
24. A process for the preparation of a compound of formula I according to claim 1, wherein Y, X, Z, P, Q, R, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, A, m and n are defined as in formula I, comprising reacting of a compound of formula **XXII**:



(XXII) (I)

wherein the reaction is being performed by activation of a compound of formula **XXII** by treatment with a coupling agent or with an acyl halide reagent followed by treatment with the appropriate amine, followed by cleavage of the solid phase moiety by treatment with an suitable acid in a suitable solvent, and where the reaction temperature is between 0 °C and reflux, to give a compound of formula I.

25. A compound of formula **XIXa**



(XIXa)

wherein

P is phenyl

R^1 and R^2 are independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylheterocycloalkyl , C_{1-6}alkylNR^6R^7, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylheterocycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl may be substituted by one or more A;

R^1 and R^2 may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

R^3 is independently selected from halogen, nitro, CHO, C_{0-6}alkylCN, OC_{1-6}alkylCN, C_{0-6}alkylOR^6, OC_{1-6}alkylOR^6, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6}alkylNR^6R^7, OC_{1-6}alkylNR^6R^7, OC_{1-6}alkylOC_{1-6}alkylNR^6R^7, NR^6OR^7, C_{0-6}alkylCO_2R^6, OC_{1-6}alkylCO_2R^6, C_{0-6}alkyl$CONR^6R^7$, OC_{1-6}alkyl$CONR^6R^7$, OC_{1-6}alkyl$NR^6(CO)R^7$, C_{0-6}alkyl$NR^6(CO)R^7$, $O(CO)NR^6R^7$, $NR^6(CO)OR^7$, $NR^6(CO)NR^6R^7$, $O(CO)OR^6$, $O(CO)R^6$, C_{0-6}alkylCOR^6, OC_{1-6}alkylCOR^6, $NR^6(CO)(CO)R^6$, $NR^6(CO)(CO)NR^6R^7$, SR^6, C_{0-6}alkyl$(SO_2)NR^6R^7$, OC_{1-6}alkyl$NR^6(SO_2)R^7$, OC_{0-6}alkyl$(SO_2)NR^6R^7$, C_{0-6}alkyl$(SO)NR^6R^7$, OC_{1-6}alkyl$(SO)NR^6R^7$, SO_3R^6, C_{0-6}alkyl$NR^6(SO_2)NR^6R^7$, C_{0-6}alkyl$NR^6(SO)R^7$, OC_{1-6}alkyl$NR^6(SO)R^7$, OC_{0-6}alkylSO_2R^6, C_{0-6}alkylSO_2R^6, C_{0-6}alkylSOR^6, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl may be optionally substituted by one or more A;

R^6 and R^7 are independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl and C_{1-6}alkylNR^8R^9;

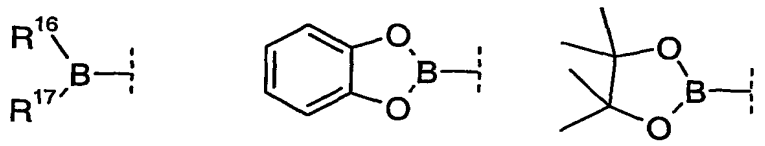
R^6 and R^7 may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A and wherein a CH_2 group may optionally be replaced by a CO group;

R^8 and R^9 are independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl;

R^8 and R^9 may together form a 5 or 6 membered heterocyclic ring containing one or more heteroatoms selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

m is 0, 1, 2, 3 or 4;

R^{15} is a group outlined in Scheme I, wherein R^{16} and R^{17} are hydroxy and B is boron;



Scheme I. Examples but not limitations of R^{15}

A is halogen, oxo (=O), nitro, CHO, CN, OR^6, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6}alkylNR^6R^7, OC_{1-6}alkylNR^6R^7, CO_2R^8, $CONR^6R^7$, $NR^6(CO)R^6$, $O(CO)R^6$, COR^6, SR^6, $(SO_2)NR^6R^7$, $(SO)NR^6R^7$, SO_3R^6, SO_2R^6 or SOR^6; as a free base or a salt, solvate or solvate of a salt thereof.

26. A compound according to claim 25, wherein

R^1 and R^2 together forms a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

m is 0;

A is C_{1-6}alkyl; as a free base or a salt, solvate or solvate of a salt thereof.

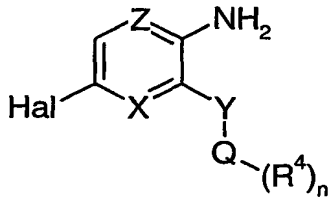
27. A compound which is

4-(Pyrrolidin-1-ylsulfonyl)phenylboronic acid;

4-[(4-Methylpiperazin-1-yl)sulfonyl]phenylboronic acid;

as a free base or a salt, solvate or solvate of a salt thereof.

28. A compound of formula IV



(IV)

wherein

Y is $CONR^5$, NR^5CO, SO_2NR^5, NR^5SO_2, CH_2NR^5 NR^5CONR^5, CH_2CO, CO or CH_2O;

X is CH or N;

Z is N;

Q is C_{1-6}alkyl, C_{2-6}alkenyl or C_{2-6}alkynyl;

R^4 is independently selected from halogen, nitro, CHO, CN, OC_{1-6}alkylCN, OR^6, OC_{1-6}alkylOR^6, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, NR^6R^7, OC_{1-6}alkylNR^6R^7, NR^6OR^7, CO_2R^6, OC_{1-6}alkylCO_2R^6, $CONR^6R^7$, OC_{1-6}alkyl$CONR^6R^7$, OC_{1-6}alkyl$NR^6(CO)R^7$, $NR^6(CO)R^7$, $O(CO)NR^6R^7$, $NR^6(CO)OR^7$, $NR^6(CO)NR^6R^7$, $O(CO)OR^6$, $O(CO)R^6$, COR^6, OC_{1-6}alkylCOR^6, $NR^6(CO)(CO)R^6$, $NR^6(CO)(CO)NR^6R^7$, SR^6, $(SO_2)NR^6R^7$, OC_{1-6}alkyl$NR^6(SO_2)R^7$, OC_{0-6}alkyl$(SO_2)NR^6R^7$, $(SO)NR^6R^7$, OC_{1-6}alkyl$(SO)NR^6R^7$, SO_3R^6, $NR^6(SO_2)NR^6R^7$, $NR^6(SO)R^7$, OC_{1-6}alkyl$NR^6(SO)R^7$, OC_{0-6}alkylSO_2R^6, SO_2R^6, SOR^6, C_{3-6}cycloalkyl, phenyl, a 5 or 6 membered heteroaromatic ring containing one or more heteroatoms independently selected from N, O, or S, or a 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O, or S which heterocyclic group may be saturated or unsaturated, and said phenyl ring or 5 or 6 membered heteroaromatic ring or 5 or 6 membered heterocyclic ring may optionally be fused with a 5 or 6 membered saturated, partially saturated or unsaturated ring containing

atoms independently selected from C, N, O or S wherein any C_{3-6}cycloalkyl, phenyl, 5 or 6 membered heteroaromatic ring with one or two heteroatoms selected independently from N, O, or S or a 5 or 6 membered heterocyclic ring containing one or two heteroatoms selected independently from N, O, or S; may be optionally be substituted by one or more A;

R^5 is hydrogen or C_{1-6}alkyl

R^6 and R^7 are independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl and C_{1-6}alkylNR^8R^9;

R^6 and R^7 may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A and wherein a CH_2 group may optionally be replaced by a CO group;

R^8 and R^9 are independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl;

R^8 and R^9 may together form a 5 or 6 membered heterocyclic ring containing one or more heteroatoms selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

Hal is halogen;

n is 0, 1, 2, 3 or 4;

A is halogen, oxo (=O), nitro, CHO, CN, OR^6, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6}alkylNR^6R^7, OC_{1-6}alkylNR^6R^7, CO_2R^8, $CONR^6R^7$, $NR^6(CO)R^6$, $O(CO)R^6$, COR^6, SR^6, $(SO_2)NR^6R^7$, $(SO)NR^6R^7$, SO_3R^6, SO_2R^6 or SOR^6;

as a free base or a salt, solvate or solvate of a salt thereof.

29. A compound according to claim 28, wherein

Y is $CONR^5$;

X is N;

Q is C_{1-6}alkyl;

R^4 is independently selected from CN, OR^6, a 5 or 6 membered heteroaromatic ring containing one or more heteroatoms independently selected from N, O, or S, or a 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected

from N, O, or S which heterocyclic group may be saturated or unsaturated, wherein any 5 or 6 membered heterocyclic ring containing one or two heteroatoms selected independently from N, O, or S; may be optionally be substituted by A;

R^5 is hydrogen;

R^6 is, C_{1-6}alkyl;

n is 1;

A is oxo (=O);

as a free base or a salt, solvate or solvate of a salt thereof.

30. A compound which is

3-Amino-6-bromo-*N*-(2-morpholin-4-ylethyl)pyrazine-2-carboxamide;

3-Amino-6-bromo-*N*-[2-(1*H*-imidazol-4-yl)ethyl]pyrazine-2-carboxamide;

3-Amino-6-bromo-*N*-[3-(1*H*-imidazol-1-yl)propyl]pyrazine-2-carboxamide;

3-Amino-6-bromo-*N*-(2-thien-2-ylethyl)pyrazine-2-carboxamide;

3-Amino-6-bromo-*N*-(thien-2-ylmethyl)pyrazine-2-carboxamide;

3-Amino-6-bromo-*N*-(2-methoxyethyl)pyrazine-2-carboxamide;

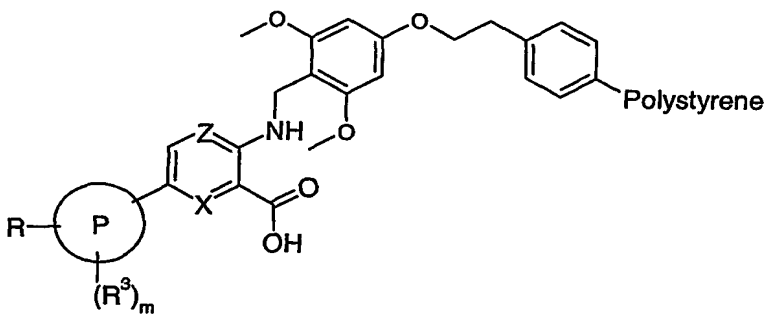
3-Amino-6-bromo-*N*-(3-methoxypropyl)pyrazine-2-carboxamide;

3-Amino-6-bromo-*N*-[3-(2-oxopyrrolidin-1-yl)propyl]pyrazine-2-carboxamide;

3-Amino-6-bromo-*N*-(cyanomethyl)pyrazine-2-carboxamide;

as a free base or a salt, solvate or solvate of a salt thereof.

31. A compound of formula **XXII**



(XXII)

wherein:

Z is N;

X is CH or N;

P is phenyl or a 5 or 6 membered heteroaromatic ring containing one or more heteroatoms selected from N, O or S and said phenyl ring or 5 or 6 membered heteroaromatic ring may optionally be fused with a 5 or 6 membered saturated, partially saturated or unsaturated ring containing atoms independently selected from C, N, O or S;

R is CHO, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6}alkyl$(SO_2)NR^1R^2$, OC_{0-6}alkyl$(SO_2)NR^1R^2$, OC_{1-6}alkyl$(SO)NR^1R^2$, C_{1-6}alkyl$(SO)NR^1R^2$, C_{0-6}alkyl$NR^1(SO)R^2$, OC_{1-6}alkyl$NR^1(SO)R^2$, C_{0-6}alkyl$NR^1(SO_2)NR^1R^2$, OC_{1-6}alkyl$NR^1(SO_2)R^2$, C_{0-6}alkyl$(SO_2)C_{1-6}$alkylNR^1R^2, OC_{0-6}alkyl$(SO_2)C_{1-6}$alkylNR^1R^2, C_{0-6}alkyl$(SO)C_{1-6}$alkylNR^1R^2, OC_{1-6}alkyl$(SO)C_{1-6}$alkylNR^1R^2, C_{0-6}alkylSC_{1-6}alkylNR^1R^2, OC_{1-6}alkylSC_{1-6}alkylNR^1R^2, OC_{1-6}alkylOC_{1-6}alkyl, C_{1-6}alkylOC_{1-6}alkylNR^1R^2, OC_{1-6}alkylOC_{1-6}alkylNR^1R^2, C_{0-6}alkyl$CONR^{10}R^{11}$, OC_{0-6}alkyl$CONR^1R^2$, OC_{1-6}alkylNR^1R^2, C_{0-6}alkyl$NR^{10}(CO)R^{11}$, OC_{1-6}alkyl$NR^1(CO)R^2$, C_{0-6}alkyl$NR^{11}(CO)R^{10}$, C_{0-6}alkylCOR^{11}, OC_{1-6}alkylCOR^1, C_{0-6}alkyl$NR^{10}R^{11}$, C_{0-6}alkyl$O(CO)R^{11}$, OC_{1-6}alkyl$O(CO)R^1$, C_{0-6}alkyl$C(NR^{10})NR^{10}R^{11}$, C_{0-6}alkyl$C(NR^{11})N(R^{10})_2$, OC_{0-6}alkyl$C(NR^1)NR^1R^2$, C_{0-6}alkyl$NR^{10}(CO)OR^{11}$, OC_{1-6}alkyl$NR^1(CO)OR^2$, C_{0-6}alkyl$NR^{11}(CO)OR^{10}$, OC_{1-6}alkylCN, NR^1OR^2, C_{0-6}alkyl$(CO)OR^8$, OC_{1-6}alkyl$(CO)OR^1$, $NR^1(CO)NR^1R^2$, $NR^1(CO)(CO)R^2$, $NR^1(CO)(CO)NR^1R^2$, OR^{12} or SO_3R^1;

R^1 and R^2 are independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylheterocycloalkyl , C_{1-6}alkylNR^6R^7, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylheterocycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl may be substituted by one or more A;

R^1 and R^2 may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

R^3 is independently selected from halogen, nitro, CHO, C_{0-6}alkylCN, OC_{1-6}alkylCN, C_{0-6}alkylOR^6, OC_{1-6}alkylOR^6, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6}alkylNR^6R^7, OC_{1-6}alkylNR^6R^7, OC_{1-6}alkylOC_{1-6}alkylNR^6R^7, NR^6OR^7, C_{0-6}alkylCO_2R^6, OC_{1-6}alkylCO_2R^6,

C_{0-6}alkylCONR^{6}R^7, OC_{1-6}alkylCONR^{6}R^7, OC_{1-6}alkylNR^6(CO)R^7, C_{0-6}alkylNR^6(CO)R^7, O(CO)NR^{6}R^7, NR^6(CO)OR^7, NR^6(CO)NR^{6}R^7, O(CO)OR^6, O(CO)R^6, C_{0-6}alkylCOR^6, OC_{1-6}alkylCOR^6, NR^6(CO)(CO)R^6, NR^6(CO)(CO)NR^{6}R^7, SR^6, C_{0-6}alkyl(SO_2)NR^{6}R^7, OC_{1-6}alkylNR^6(SO_2)R^7, OC_{0-6}alkyl(SO_2)NR^{6}R^7, C_{0-6}alkyl(SO)NR^{6}R^7, OC_{1-6}alkyl(SO)NR^{6}R^7, SO_3R^6, C_{0-6}alkylNR^6(SO_2)NR^{6}R^7, C_{0-6}alkylNR^6(SO)R^7, OC_{1-6}alkylNR^6(SO)R^7, OC_{0-6}alkylSO_2R^6, C_{0-6}alkylSO_2R^6, C_{0-6}alkylSOR^6, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl, wherein any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl may be optionally substituted by one or more A;

R^6 and R^7 are independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl and C_{1-6}alkylNR^{8}R^9;

R^6 and R^7 may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S, which heterocyclic ring may be optionally substituted by A and wherein a CH_2 group may optionally be replaced by a CO group;

R^8 and R^9 are independently selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl and C_{0-6}alkylheteroaryl;

R^8 and R^9 may together form a 5 or 6 membered heterocyclic ring containing one or more heteroatoms selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

R^{10} is hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, C_{0-6}alkylheteroaryl or C_{1-6}alkylNR^{8}R^9;

R^{11} is C_{1-6}alkylNR^{8}R^9;

R^{10} and R^{11} may together form a 5 or 6 membered heterocyclic ring containing one or more heteroatoms selected from N, O or S, which heterocyclic ring may be optionally substituted by A;

A is halogen, oxo (=O), nitro, CHO, CN, OR^6, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, fluoromethyl, difluoromethyl, trifluoromethyl, fluoromethoxy, difluoromethoxy, trifluoromethoxy, C_{0-6}alkylNR^{6}R^7, OC_{1-6}alkylNR^{6}R^7, CO_2R^8, CONR^{6}R^7, NR^6(CO)R^6, O(CO)R^6, COR^6, SR^6, (SO_2)NR^{6}R^7, (SO)NR^{6}R^7, SO_3R^6, SO_2R^6 or SOR^6;

m is 0, 1, 2, 3 or 4;

as a free base or a salt, solvate or solvate of a salt thereof.

32. A compound according to claim 31, wherein:

X is N;

P is phenyl;

R is C_{0-6}alkyl$(SO_2)NR^1R^2$;

R^1 and R^2 may together form a substituted 5 or 6 membered heterocyclic ring containing one or more heteroatoms independently selected from N, O or S;

m is 0;

as a free base or a salt, solvate or solvate of a salt thereof.

33. A compound which is

Methyl 3-{[2,6-dimethoxy-4-(2-phenylethoxy)benzyl]amino}-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxylate polystyrene;

3-{[2,6-Dimethoxy-4-(2-phenylethoxy)benzyl]amino}-6-[4-(pyrrolidin-1-ylsulfonyl)phenyl]pyrazine-2-carboxylic acid polystyrene;

as a free base or a salt, solvate or solvate of a salt thereof.

34. The use of the intermediates according to any one of claims to 25 to 33 for the preparation of a compound of formula **I** as defined in any one of claims 1 to 7.